



## Article

# Ezetimibe-Loaded Nanostructured Lipid Carrier Based Formulation Ameliorates Hyperlipidaemia in an Experimental Model of High Fat Diet

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**Abstract:** Ezetimibe (EZE) possesses low aqueous solubility and poor bioavailability and in addition, its extensive hepatic metabolism supports the notion of developing a novel carrier system for EZE. Ezetimibe was encapsulated into nanostructured lipid carriers (EZE-NLCs) via a high pressure homogenization technique (HPH). A three factor, two level (2<sup>3</sup>) full factorial design was employed to study the effect of amount of poloxamer 188 (X1), pressure of HPH (X2) and number of HPH cycle (X3) on dependent variables. Particle size, polydispersity index (PDI), % entrapment efficiency (%EE), zeta potential, drug content and in-vitro drug release were evaluated. The optimized formulation displays pragmatic inferences associated with particle size of 134.5 nm; polydispersity index (PDI) of 0.244 ± 0.03; zeta potential of −28.1 ± 0.3 mV; % EE of 91.32 ± 1.8% and % CDR at 24-h of 97.11%. No interaction was observed after X-ray diffraction (XRD) and differential scanning calorimetry (DSC) studies. EZE-NLCs (6 mg/kg/day p.o.) were evaluated in the high fat diet fed rats induced hyperlipidemia in comparison with EZE (10 mg/kg/day p.o.). Triglyceride, HDL-c, LDL-c and cholesterol were significantly normalized and histopathological evaluation showed normal structure and architecture of the hepatocytes. The results demonstrated the superiority of EZE-NLCs in regard to bioavailability enhancement, dose reduction and dose-dependent side effects.

**Keywords:** ezetimibe; NLCs; hyperlipidemia; high fat diet; lipid profile

## 1. Introduction

Hypercholesterolemia (hyperlipidemia) affects an enormous population. This condition is determined with a decline high density lipoprotein (HDL) levels (cholesterol < 40 mg/dL) and increased levels of low density lipoprotein (LDL) (cholesterol > 190 mg/dL) along with triglycerides (TG) in plasma (>200 mg/dL), which eventually results in the progression to atherosclerosis [1]. Excessive cholesterol, however, puts a person at risk of developing heart disease [2]. Hypercholesterolemic patients, because of excess cholesterol in the blood stream, may lead to excessive deposition of cholesterol on the walls of coronary arteries which supply blood to the heart (coronary arteries) [3].

Ezetimibe is a cholesterol absorption inhibitor drug used for the treatment of primary hypercholesterolemia. Ezetimibe decreases raised levels of high total cholesterol



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